THE ACTION OF SODIUM SULPHOCYANATE IN TUBERCULOSIS

STUDIES ON THE BIOCHEMISTRY AND CHEMOTHERAPY OF TUBERCULOSIS, XII*

HARRY J. CORPER

(From the Otho S. A. Sprague Memorial Institute and the Pathological Laboratory of the University of Chicago.)

A chemotherapeutic agent, to be of value in tuberculosis, must either produce a "Therapia magna sterilisans" in the Ehrlich sense, or must inhibit the development of the tubercle bacillus to such an extent that further growth is impossible. In order to produce either of the above, it is necessary for the chemotherapeutic agent to enter the diseased tissues in concentrations sufficient to produce either a bactericidal or an inhibitory effect, and this without material injury to the host. It is conceivable that a chemotherapeutic agent, which enters the diseased tissues, may enter, as do crystalloids, in concentration nearly equal to that in the blood, or may enter in low concentrations harmless to the host and gradually accumulate in the diseased tissues in concentrations to be bactericidal or inhibitory, altho the latter is not highly probable since a chemotherapeutic agent, which enters a tissue by way of the blood, will probably also pass out the same way as the concentration in the blood diminishes. Since we are aware, however, of such conditions as chemical affinities, this factor must be borne in mind as a possible reality. It is known, at least, that calcium salts are deposited in old tubercles and remain there in concentration far above that in the blood or body fluids. If the chemotherapeutic agent enters in concentration nearly equal to that in the blood, it should remain there, without harm to the host, in concentration sufficient to be bactericidal for a sufficient length of time, or if in concentration sufficient to be inhibitory, repeated introduction must keep up the inhibitory concentration until a permanent effect has been produced or until the host is in such a condition that further immediate development of the disease is impossible.

With these facts in mind, the study of a number of chemotherapeutic agents was undertaken, among these sodium sulphocyanate.

* Received for publication September 23, 1914.

Sodium sulphocyanate was chosen on account of its almost complete lack of toxicity toward animals, its relation to the highly toxic cyanids, its simple crystalline character, and its simplicity in chemical determinations.

LITERATURE

The toxicity of the alkali sulphocyanates was studied throroughly by Franz,[1] who believes that they possess no toxic action toward the animals studied (guinea-pig, rabbit, dog, and cat) not attributable to mere salt action, and concludes that they cannot be considered poisons in the ordinary sense. The lethal dose of potassium sulphocyanate to rabbits, given per os, was about 0.5 gm. per kilo, which was fatal in 3.5-4 days (0.9 gm. was fatal in about 6 hours). Guinea-pigs, given per os 0.6 gm. sodium sulphocyanate per kilo, died in 0.5-1 day, while 0.8 gm. was fatal in about 4 hours. One gram potassium sulphocyanate, given subcutaneously to dogs (weighing 5.7-7.8 kilos), caused no toxic symptoms. The intravenous injection of 0.25-0.5 gm. sodium sulphocyanate into dogs (6-8 kilos) was without effect.

The fact that potassium sulphocyanate was distributed, after feeding, throughout nearly the entire organism was noted by Albert,[2] tho only in a qualitative way. He states: "I have tried the ingestion of pure potassium sulphocyanid (sulphocyanate) in four rabbits, using daily between 1 and 2 gm. mixed with about ten of bran. In every case, death resulted in about a week. The symptoms produced were alike, viz., emaciation and loss of hair. In two, a marked atrophy of the salivary glands was found, and in one of these, after dipping in a solution of ferric perchlorid, a microscopic examination was made, the ducts being found more deeply stained than the gland tissue. In all four, large quantities were found in the urine and feces; in fact, the drug seemed to permeate, as far as one was able to judge, every organ and tissue, and to find its way in every secretion and excretion even to the cerebrospinal fluid."

Pollak[3] noted that, after the subcutaneous administration of sodium sulphocyanate to dogs (about 1 gm.) and rabbits (0.2-0.5 gm.), and when given per os to dogs (about 1 gm.) and man (about 2 gm.), the entire quantity was excreted in the urine in from 4-5 days. The animals tolerated the above amounts without reaction. DeSouza[4] observed that sulphocyanates pass from the blood into the saliva, pancreatic juice, bile, and urine. The concentration in the urine may be greater or less than that in the blood. After feeding sodium sulphocyanate, 82, 26.7, and 39.8 percent of that given with the food was still in the body 21, 44 and 47 hours, respectively, after ingestion. In one experiment on a dog, 22.5 percent of 3 gm. given with food remained in the body 72 hours after ingestion. Edinger and Clemens[5] analyzed the organs of a man, given 0.5 gm. sodium sulphocyanate daily for 5 days before death, and found 2 mg. in the liver, 14 mg. in the pancreas, 11 mg. in the kidneys, and practically none in the salivary glands.

Two conflicting reports were found in the literature on the effect of sodium sulphocyanate on tuberculosis; one by Martinotti,[6] who states that tubercle bacilli (variety not given) were injected into the anterior chambers of rabbits' and guinea-pigs' eyes, typical tubercles were allowed to develop and the animals

1. Arb. a. d. k. Gsndhtsamte., 1911, 38, p. 435.
2. Lancet, 1898, 1, p. 494.
3. Beitr. z. chem. Phys. u. Path., 1902, 2, p. 430.
4. Jour. Physiol., 1906, 35, p. 332.
5. Ztschr. f. klin. Med., 1906, 59, p. 218.
6. Centralbl. f. Bakteriol., Abt. I, 1896, 19, p. 142.

were then treated with sodium sulphocyanate, subcutaneous injections two or three times daily (amounts not given). The animals were completely cured and when after many months they were killed, they revealed no trace of tuberculous infection either in the eye or other organs, while controls rapidly died. The other report was by Treupel and Edinger[7] whose associate, Schlegel, found that, in culture experiments on serum and glycerin agar, tubercle bacilli (variety not given) grew vigorously in the presence of 0.6, 0.12, and 0.25 percent sodium sulphocyanate, but in the presence of 0.5 and 1 percent only sparse growth occurred. In animal experiments on guinea-pigs and rabbits, entirely negative results were obtained. The guinea-pigs were given subcutaneous injections of 0.01 gm. sodium sulphocyanate daily for five to six weeks before and continued after infection in one series, and five injections of 0.025 gm. daily after infection in another series, while the rabbits received subcutaneously 0.1 gm. sodium sulphocyanate daily for five weeks previous to and continued after infection. The type of tubercle bacilli was not stated, but was probably the bovine bacilli as indicated by the character of the disease produced in the animals.

TOXICITY OF SODIUM SULPHOCYANATE

On account of the lack of accurate data in the literature (at least none such was found) on the intravenous toxicity of sodium sulphocyanate, it was necessary to determine this in order to obtain our

TABLE 1

INTRAVENOUS TOXICITY OF SODIUM SULPHOCYANATE TO RABBITS*

Weight of Animal in Grams	Amount of Injection	Amount in Grams per Kilo	Results
1,300.....	0.3 gm. in 3.0 c.c.	0.23	Alive on fourth day, emaciated (950 gm.). Dead on fifth day
2,100.....	0.75 gm. in 7.5 c.c.	0.35	Lost weight (fourth day 1,750 gm.)
(17 days later)	1.00 gm. in 10 c.c.	0.47	(1,900 gm.). Alive
1,350.....	0.5 gm. in 5 c.c.	0.37	Much emaciated, dead on eighth day
1,300.....	0.5 gm. in 5 c.c.	0.38	(Fourth day 1,300 gm.). Dead fifth day after last injection
(11 days later)	1.0 gm. in 10 c.c.	0.76	
2,400.....	1.0 gm. in 10 c.c.	0.41	Alive.
2,240.....	1.0 gm. in 10 c.c.	0.44	Dead in 14 hours and 45 minutes
2,000.....	1.0 gm. in 10 c.c.	0.50	Dead on fourth day
1,740.....	1.0 gm. in 10 c.c.	0.57	Dead in 8 hours and 45 minutes
1,700.....	1.0 gm. in 10 c.c.	0.58	Alive
1,700.....	1.0 gm. in 10 c.c.	0.58	Alive
1,250.....	0.75 gm. in 7.5 c.c.	0.60	(Fourth day 1,200 gm.). Alive
(11 days later)	1.0 gm. in 10 c.c.	0.80	
2,270.....	1.5 gm. in 15 c.c.	0.66	Dead in 4 hours and 25 minutes
1,300.....	1.0 gm. in 10 c.c.	0.76	Dead in less than 16 hours
1,740.....	1.5 gm. in 15 c.c.	0.86	Dead in 1 hour and 45 minutes
2,240.....	2.0 gm. in 20 c.c.	0.89	Dead in 1 hour and 20 minutes
1,890.....	2.0 gm. in 20 c.c.	1.05	Dead in 2 minutes

* In all the experiments in this paper, it was considered sufficiently accurate to use pure crystals of sodium sulphocyanate (which show no signs of deliquescence and have been kept in paraffin-stoppered bottles), and all the weights given indicate the amount of pure crystals rather than the absolute amount of sulphocyanate which could be obtained only by frequent quantitative chemical analyses. Therefore, the figures are relative rather than absolute.

7. München. med. Wchnschr., 1900, 47, p. 767.

figures on the highest concentration that can be attained in the tissues without material injury to the host. With a simple crystalline salt, as sodium sulphocyanate, the intravenous lethal dose is the only gauge that can be used, since it is desirable to avoid the local toxic action such as might occur by giving large amounts per os or subcutaneously. By the intravenous route, an almost immediate dilution of the salt occurs and thus only the systemic toxicity is obtained. The results of these experiments are shown in Table 1.

The principal immediate symptoms noted, when toxic doses of sodium sulphocyanate were given, were a muscular rigidity and paralysis of the hind legs, irregular, rapid, or slow-labored respiration, and toward the end, when death occurred, coma. Emaciation was one of the principal remote symptoms when the animal survived for a few days.

Table 1 shows that the acute lethal dose for a 1 kilo rabbit was about 0.4-0.6 gm. of sodium sulphocyanate, given intravenously. Delayed death (after the fifth day) may occur in exceptional cases, however, even with smaller doses.

CONCENTRATION OF SODIUM SULPHOCYANATE IN THE TISSUES

With the systemic lethal dose of sodium sulphocyanate now known, it was possible to determine the maximum concentration obtainable in the tissues, mainly the tubercles.

Method of Analysis.—The following quantitative colorimetric method of analysis was used because of its simplicity and sufficient relative, rather than absolute, accuracy to determine the large amounts of sodium sulphocyanate which interest us in this problem (absolute accuracy not being necessary).

The sample of tissue (1-5 gm.) to be analyzed was placed in about 75-100 c.c. of 95 percent alcohol and ground up, allowed to remain in a cool place with frequent shaking for twenty-four hours, and then filtered through a dry filter paper, the precipitate washed two or three times with small amounts of 95 percent alcohol, the filtrate evaporated to dryness on the water bath and, after cooling, the residue extracted (by stirring with a glass rod) by means of 3-4 portions of 3-5 c.c. of 95 percent alcohol, and filtered. To the filtrate (or fraction thereof) diluted to a definite volume (10 c.c.) was added 0.1 c.c. ferric chlorid (30 percent) solution and it was vigorously shaken. The addition of the ferric chlorid frequently results in the formation of a turbidity, which separates on shaking or may be removed by filtration through a dry filter paper. The resulting solution was then placed in the chamber of a DuBosc colorimeter and compared with a standard solution of sodium sulphocyanate in 95 percent alcohol, containing from 0.2-2.0 mg. sodium sulphocyanate in 10 c.c., to which had been added 0.1 c.c. ferric chlorid solution (30 percent).

The delicacy of this method decreased with decreasing amounts of sodium sulphocyanate on account of the interfering color produced by the 0.1 c.c. (30 percent) ferric chlorid. Tested in the DuBosc colorimeter, using 10 c.c. 95

percent alcohol as solvent, this color corresponded to a reading of 0.04 mg., using 0.2 mg. sodium sulphocyanate for comparison. The interference was barely appreciable when over 0.2 mg. sodium sulphocyanate was present.

Control Analysis to Test the Accuracy of the Method.—In order to test the accuracy of the method just described, 1.0 mg. sodium sulphocyanate was added to samples of a rabbit's organs and these were then analyzed. The results were as follows:

6.5 and 7.5 gm. of blood yielded, respectively....1.0 and 0.95 mg. NaSCN.
5.0 and 5.0 gm. of liver yielded, respectively....0.77 and 0.60 mg. NaSCN.
6.0 and 6.5 gm. of kidney yielded, respectively...0.86 and 0.85 mg. NaSCN.
5.2 and 3.7 gm. of lung yielded, respectively.....0.84 and 0.76 mg. NaSCN.
2.8 and 2.8 gm. of eye yielded, respectively.....0.80 and 0.91 mg. NaSCN.
5.2 gm. of heart yielded.....0.80 mg. NaSCN.

Controls, using 4-5 gm. of tissue (kidney, heart, and lung) to which had been added 0.4 and 0.6 mg. sodium sulphocyanate, carried through the entire method, revealed a recovery of about 70 percent.

Duration of Sodium Sulphocyanate in the Blood After Intravenous Injection.—A rabbit (2,100 gm.) was given in the marginal ear vein 0.75 gm. of sodium sulphocyanite in 7.5 c.c. of distilled water fifteen minutes after withdrawing 5 gm. of blood from the heart for control analysis. At intervals thereafter, other samples were taken from the heart and analyzed for sodium sulphocyanate content colorimetrically by the method given above with the following results:

The normal sample contained no sulphocyanate.
4.1 gm. taken thirty minutes after injection of the sodium sulphocyanate contained 0.88 mg. per gram of blood.
4.6 gm. taken eighteen hours after injection contained 0.59 mg. per gram.
4.3 gm. taken twenty-three hours after injection contained 0.57 mg. per gram.
7.1 gm. taken 66 hours after injection contained 0.47 mg. per gram.
6.7 gm. taken 92 hours after injection contained 0.23 mg. per gram.
7.1 gm. taken 116 hours after injection contained 0.014 mg. per gram.
7.0 gm. taken 140 hours after injection contained 0.000 mg. per gram.

This experiment shows that sodium sulphocyanate (0.36 gm. per kilo) given intravenously to rabbits is present in the blood in appreciable amounts up to the fifth day after administration.

As sodium sulphocyanate given intravenously can be present in the blood for at least 5 days, it is significant in what concentrations and how long it remains in the tissues of the body. Is there any evidence of a chemical affinity for any of these tissues? With these questions in mind the following experiments were performed.

The analyses were carried out in duplicate when enough tissue was available for this purpose (that is, provided the organs analyzed weighed more than 3-5 gm.).

Experiment 1.—A rabbit (2,500 gm.) with a well-developed tuberculosis * of the right eye involving the entire bulb was given intravenously, into the

* In all the experiments in this paper the human type of tubercle bacilli was used.

marginal ear vein, 1 gm. of sodium sulphocyanate in 10 c.c. sterile distilled water and was bled to death four hours after the injection. All the organs were normal. The tissues were analyzed with the following results: The blood contained 0.82 mg. sodium sulphocyanate per 1 gm.; the liver (66 gm.) 0.20 mg.; the left lung (3.0 gm.) 0.52 mg.; the right lung (4 gm.) 0.50 mg.; the heart (7 gm.) 0.46 mg.; right kidney (8 gm.) 0.30 mg.; left kidney (8 gm.) 0.30 mg.; testes (6 gm.) 0.46 mg.; tuberculous right eye (4 gm.) 0.67 mg.; and the normal left eye (4 gm.) 0.45 mg.

Experiment 2.—A rabbit (2,420 gm.) was injected intramuscularly with dead fat-free tubercle bacilli (which produced a typical sterile tubercle) and, after development of nodules of 4-5 gm., was given intravenously 1 gm. sodium sulphocyanate in 10 c.c. sterile distilled water. The animal was bled to death twenty-four hours after the injection of the sodium sulphocyanate and the tissues were analyzed with the following results: The blood taken fifteen minutes before injection (for control) contained no sulphocyanate, one hour after injection 0.90 mg. per 1 gm., twenty-four hours (when the animal was killed) after injection 0.62 mg.; the liver (52 gm.) contained 0.25 mg.; right lung (4.7 gm.) 0.46 mg.; left lung (3.5 gm.) 0.57 mg.; heart (5.5 gm.) 0.40 mg.; right kidney (6.8 gm.) 0.35 mg.; left kidney (7.0 gm.) 0.27 mg.; the urine found in the bladder 0.60 mg.; testes (7.4 gm.) 0.36 mg.; normal right eye (3.3 gm.) 0.51 mg.; normal left eye (3.0 gm.) 0.52 mg.; a necrotic nodule in the left fore leg (4.4 gm.) 0.75 mg.; a necrotic nodule in the right fore leg (4.0 gm.) 0.65 mg.; normal muscle from the left fore leg 0.08 mg.; normal muscle from the right fore leg 0.08 mg.; and normal muscle from left hind leg 0.10 mg.

Experiment 3.—A rabbit (2,800 gm.) with a fairly well developed tuberculosis of the right eye was given intravenously 0.9 gm. sodium sulphocyanate in 9 c.c. sterile distilled water and was bled to death three days after the injection. All the organs were normal. The tissues were analyzed with the following results: The blood contained 0.65 mg. sodium sulphocyanate per 1 gm.; liver (52 gm.) 0.28 mg.; right lung (3.8 gm.) 0.52 mg.; left lung (3.5 gm.) 0.47 mg.; heart (4.8 gm.) 0.37 mg.; right kidney (5.2 gm.) 0.32 mg.; left kidney (5.5 gm.) 0.37 mg.; the tuberculous right eye (3.2 gm.) 0.56 mg.; normal left eye (3.4 gm.) 0.53 mg.; normal muscle of right hind leg 0.06 mg.; and the normal muscle of the left hind leg 0.06 mg.

Experiment 4.—A rabbit (2,830 gm.) with a well-developed tuberculosis of the right eye was given intravenously 0.9 gm. sodium sulphocyanate in 9 c.c. sterile distilled water and died four days later. The left lung contained 0.38 mg. sodium sulphocyanate per 1 gm.; the right lung 0.38 mg.; right kidney 0.26 mg.; left kidney 0.24 mg.; the tuberculous right eye 0.46 mg.; and the normal left eye 0.41 mg.

Experiment 5.—A rabbit (2,800 gm.) was injected intramuscularly with dead fat-free tubercle bacilli, and, after development of good-sized nodules, was given intravenously 0.75 gm. sodium sulphocyanate in 7.5 c.c. sterile distilled water. The animal was bled to death five days after the injection of the sodium sulphocyanate and the tissues were analyzed with the following results: The blood contained 0.03 mg. sodium sulphocyanate per 1 gm.; the liver (89 gm.) 0.01 mg.; right lung (6.5 gm.) 0.02 mg.; left lung (5.6 gm.) 0.02 mg.; heart (7.5 gm.) 0.02 mg.; mammary glands 0.02 mg.; right kidney (8.4 gm.) 0.02 mg.; left kidney (8.6 gm.) 0.03 mg.; normal right eye (3.5 gm.) 0.03 mg.; normal left eye (4.0 gm.) 0.03 mg.; a necrotic nodule in the right fore leg (9.7 gm.) 0.02 mg.; a necrotic nodule in the left fore leg (13.5 gm.) 0.02 mg.; a necrotic

nodule in the right hind leg (7.5 gm.) 0.02 mg.; caseous material (4.0 gm.) from a nodule in the left hind leg 0.04 mg.; capsule (3.5 gm.) of this nodule 0.04 mg.; and normal muscle from the right hind leg 0.01 mg.

Experiment 6.—A rabbit (2,400 gm.) with a large acute abscess was given 1.0 gm. sodium sulphocyanate intravenously and bled to death after two days. the blood contained 0.57 mg. sodium sulphocyanate per 1 gm. and the pus contained 0.59 mg.

Experiments 7 and 8.—Two guinea-pigs (about 400 gm.) with well-advanced generalized tuberculosis (enlarged inguinal, retroperitoneal, and peribronchial lymph glands, liver full of numerous necrotic areas, spleen enlarged and containing large areas of necrosis, and lungs containing numerous small foci of necrosis) were given subcutaneously 0.5 gm. sodium sulphocyanate in 5 c.c. sterile distilled water and killed about three hours after the injection of the

TABLE 2

DISTRIBUTION OF SODIUM SULPHOCYANATE IN THE TISSUES OF TUBERCULOUS RABBITS AT VARIOUS INTERVALS AFTER INTRAVENOUS INJECTIONS

Experiment	NaSCN Given per Kilo	Time Between Analysis and Injection	Amount of Sulphocyanate in Milligrams													
			Blood	Liver	Right Kidney	Left Kidney	Heart	Testes	Right Lung	Left Lung	Normal Eye	Tubercular Eye	Normal Muscle	Tuberculous Nodule from Muscle	Pus
1.....	0.4	4 hrs.	0.82	0.20	0.30	0.30	0.46	0.46	0.50	0.52	0.45	0.67	.....	.....	....
2.....	0.41	24 hrs.	0.62	0.25	0.35	0.27	0.40	0.36	0.46	0.57	R. 0.51 ..... L. 0.52	.....	0.08 0.08 0.10	0.75 ..... 0.65	....
3.....	0.32	3 days	0.65	0.28	0.32	0.37	0.37	.....	0.52	0.47	0.53	0.56	0.06 ..... 0.06	.....	....
4.....	0.32	4 days	.....	.....	0.26	0.24	.....	.....	0.38	.....	0.41	0 46	.....	.....	....
5.....	0.27	5 days	0.03	0.01	0.02	0.03	0.02	.....	0.02	0.02	R. 0.03 ..... L. 0.03	.....	0.01	0.02 0.02 0.04	....
6.....	0.41	2 days	0.57	.....	.....	....	.....	.....	.....	.....	.....	.....	.....	.....	0.59

sodium sulphocyanate. The tissues were analyzed with the following results: The blood contained 1.66 and 1.04 mg. sodium sulphocyanate per 1 gm.; the liver (16 and 25 gm.) 0.62 and 1.11 mg.; the spleen (3 and 2.5 gm.) 0.52 and 0.80 mg.; lungs (4 and 8 gm.) 0.62 and 0.62 mg.; kidneys (3.0 and 3.5 gm.) 0.50 and 0.46 mg.; the inguinal glands (2.5 and 2.5 gm.) 0.52 and 0.64 mg.; the retroperitoneal glands (1.0 and 1.5 gm.) 1.56 and 1.40 mg.; and the peribronchial glands (1.5 and 1.5 gm.) 1.0 and 1.1 mg., respectively.

Sodium sulphocyanate, a simple crystalloid, given intravenously to rabbits is therefore found in high concentration, about the same as that of the blood, in the tubercle (tuberculous eye of the rabbit, necrotic tissues produced by dead fat-free tubercle bacilli in the muscles of rabbits, and tuberculous tissues of the guinea-pig), the normal eye,

lungs, kidneys, heart, and testes. The liver generally contains less than the blood and other organs, and the normal muscle contains only traces. These results agree well with those of Wells and Hedenburg,[8] who found that simple crystalloids (potassium iodid) enter necrotic tissues to reach about the same concentration as in the blood. They also bear evidence in favor of the statement made by these authors that simple crystalloids are well suited as entrants into the tubercle. Pus from acute abscesses in rabbits also contains large amounts of sodium sulphocyanate, about equal to the amount in the blood after injection. The sodium sulphocyanate, in the tissues and tubercles, disappears as rapidly as it does from the blood and is practically absent after 5 days. No evidence of a chemical affinity for any of the tissues was obtained.

TUBERCULOCIDAL ACTION OF SODIUM SULPHOCYANATE

In order to determine whether or not sodium sulphocyanate possessed any bactericidal properties, 10 drops of a heavy emulsion of tubercle bacilli were added to 5 c.c. of varying concentrations — 1.0, 0.5, 0.1, 0.01, and 0.001 percent of sodium sulphocyanate (distilled water was used as solvent in the higher and 0.9 percent salt solution in the lower concentrations) in duplicate and placed in the incubator at 37 C. for 48 hours. Six controls were made at the same time, three with distilled water, and three with 0.9 percent sodium chlorid. At the end of this time, the entire solution (in the case of the higher concentrations, the sediment only was used) was injected subcutaneously into normal guinea-pigs. It suffices to state that all the guinea-pigs developed a tuberculosis. Even the 1 percent sodium sulphocyanate did not attenuate the bacilli in this length of time.

Similarly, human tubercle bacilli were exposed to 0.1, 0.01, and 0.001 percent sodium sulphocyanate for 7 days at 37 C., being injected into normal guinea-pigs at the end of this time. All of the guinea-pigs developed a tuberculosis.

SUMMARY

Sodium sulphocyanate is lethal to rabbits when given intravenously in amounts of 0.4-0.6 gm. per kilo. Delayed death may occur even from smaller amounts.

When injected intravenously (about 0.4 gm. per kilo), it is found in the tuberculous tissues in concentration about equal to that in the

8. Jour. Infect. Dis., 1912, II, p. 349.

blood (0.06-0.08 percent). The concentration in the lungs, heart, kidneys, and testes is not far from that in the blood, the concentration in the liver is less, while it is practically absent from the muscles. It disappears from the tissues (normal and tuberculous) as speedily as it does from the blood (being absent about 5 days after injection). No evidence of a chemical affinity of the sodium sulphocyanate for any of the normal or tuberculous tissues was obtained. Tubercle bacilli, exposed to concentrations of sodium sulphocyanate up to 1 percent for 48 hours at 37 C. and up to 0.1 percent for 7 days at 37 C., were not killed. No evidence even of attenuation was observed.